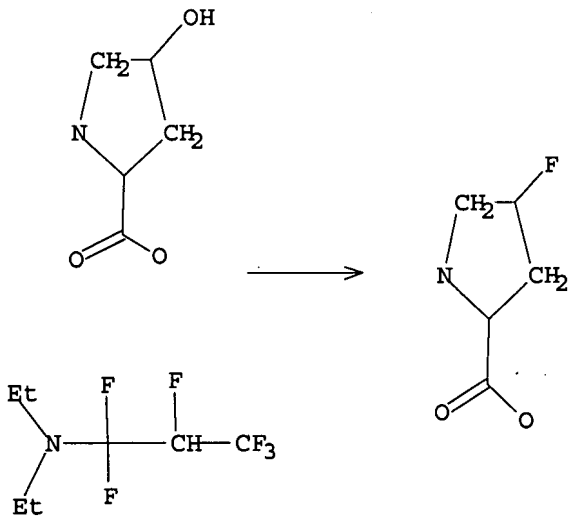
=> d his

(FILE 'HOME' ENTERED AT 14:23:27 ON 23 MAY 2007)

FILE 'CASREACT' ENTERED AT 14:23:44 ON 23 MAY 2007
L1 STRUCTURE UPLOADED
L2 0 S L1
L3 3 S L1 FULL

=> d que l3 stat
L1 STR



Structure attributes must be viewed using STN Express query preparation.
L3 3 SEA FILE=CASREACT SSS FUL L1 (10 REACTIONS)

100.0% DONE 12 VERIFIED 10 HIT RXNS 3 DOCS
SEARCH TIME: 00.00.01

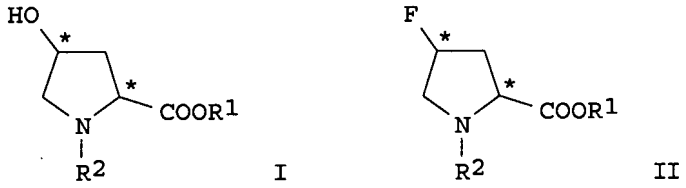
=> d 1-3 bib abs fhit

L3 ANSWER 1 OF 3 CASREACT COPYRIGHT 2007 ACS on STN
AN 145:397782 CASREACT
TI Process for production of optically active fluoroproline derivative
IN Kondo, Norihisa; Watanabe, Akio; Kanezaki, Hiroki; Kawada, Kosuke
PA Tosoh F-Tech, Inc., Japan
SO PCT Int. Appl., 23pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006103986	A1	20061005	WO 2006-JP305674	20060322

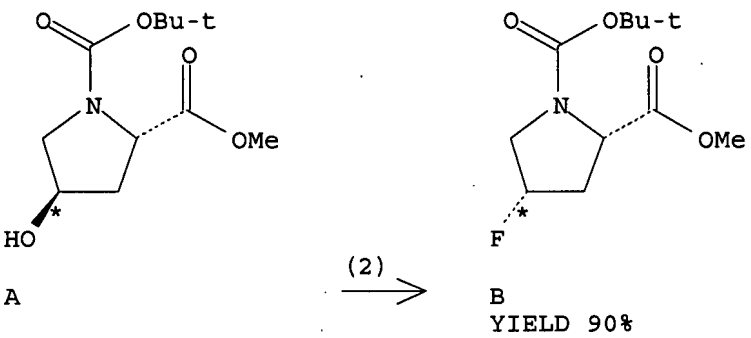
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI JP 2005-92878 20050328
OS MARPAT 145:397782
GI



AB There is provided a process for producing an optically active fluoroproline derivative represented by the general formula (I; R1 = substituted or unsubstituted alkyl or aryl group; R2 = substituted or unsubstituted alkyl, aryl, alkylcarbonyl, alkoxycarbonyl, arylcarbonyl or aryloxycarbonyl group; an asterisk (*) denotes an asym. carbon) by fluorinating an optically active hydroxyproline derivative represented by the general formula (II; R1 , R2 = same as above). The process comprises adding N-(2-chloro-1,1,2-trifluoroethyl) diethylamine (CTT) or N-(1,1,2,3,3,3-hexafluoropropyl)diethylamine (PPDA) which is inexpensive and easy to handle to an aprotic nonpolar organic solvent at a temperature of 10° or lower and then fluorinating the compound I at a temperature ranging from 10 to 50°. This process enables to produce an optically active fluoroproline derivative represented by the general formula II in which the configuration at position-4 of a compound represented by the general formula I is inverted, in a high purity with reduced production of byproducts, e.g. chloroproline derivs. when CTT is used as the fluorinating agent. Thus, 4.91 g N-(tert-butoxycarbonyl)-(2S,4R)-4-hydroxyproline Me ester and 0.14 g ethanol were dissolved in 18 g CHCl3, cooled to -10°, followed by adding 4.55 g CTT, and the reaction liquid was warmed to 30°, and stirred for 15 h to give 89% N-(tert-butoxycarbonyl)-(2S,4S)-4-fluoroproline Me ester (97.8% purity).

RX(2) OF 2 A ===> B



A

B
YIELD 90%

RX(2) RCT A 74844-91-0
RGT F 309-88-6 Ishikawa reagent
PRO B 203866-16-4
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C -> 10 deg C
SUBSTAGE(2) 20 hours, 50 deg C
NTE fluorination

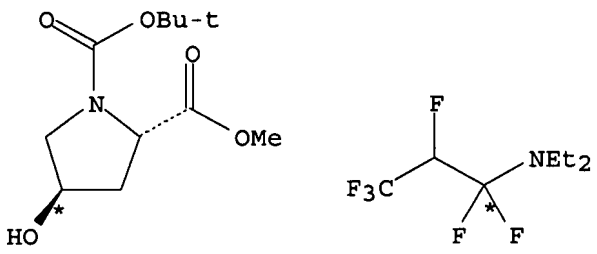
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 3 CASREACT COPYRIGHT 2007 ACS on STN
AN 142:261782 CASREACT
TI Process for preparation of cis-4-fluoro-L-proline derivatives
IN Tomisawa, Kazuyuki; Tatsuta, Dai; Yoshida, Tomomichi; Yokoo, Chihiro
PA Taisho Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

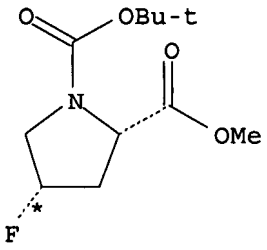
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005016880	A1	20050224	WO 2004-JP11827	20040818
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004265182	A1	20050224	AU 2004-265182	20040818
	CA 2534884	A1	20050224	CA 2004-2534884	20040818
	EP 1657237	A1	20060517	EP 2004-771788	20040818
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
	CN 1839120	A	20060927	CN 2004-80023726	20040818
	NO 2006000703	A	20060313	NO 2006-703	20060214
	US 2006281927	A1	20061214	US 2006-568708	20060804
PRAI	JP 2003-207718		20030818		
	WO 2004-JP11827		20040818		

OS MARPAT 142:261782
AB This invention pertains to a method for producing high purity cis-4-fluoro-L-proline derivs., which comprises reacting a trans-4-hydroxy-L-proline derivative with N,N-diethyl-N-(1,1,2,3,3,3-hexafluoropropyl)amine in the presence of a HF scavenger. For example, (2S,4R)-1-(tert-butoxycarbonyl)-4-hydroxypyrrolidine-2-carboxylic acid Me ester was reacted with N,N-diethyl-N-(1,1,2,3,3,3-hexafluoropropyl)amine in CH2Cl2 in the presence of NaF to give (2S,4S)-1-(tert-butoxycarbonyl)-4-fluoropyrrolidine-2-carboxylic acid Me ester. This invention provides a convenient method to prepare cis-4-fluoro-L-proline derivs. in high yield under mild conditions at low cost.

RX(1) OF 29 A + B ===> C...



A B



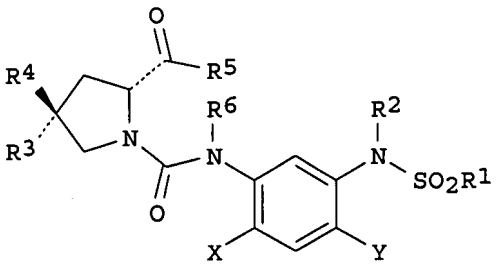
C
YIELD 85%

RX(1) RCT A 74844-91-0, B 309-88-6
RGT D 7681-49-4 NaF
PRO C 203866-16-4
SOL 75-09-2 CH2Cl2
CON SUBSTAGE(1) 0 deg C
SUBSTAGE(2) 0 deg C -> room temperature
SUBSTAGE(3) 20 hours, room temperature
NTE alternative prepn. shown
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 3 CASREACT COPYRIGHT 2007 ACS on STN
AN 129:202944 CASREACT
TI Preparation of intermediates and 1,3-dioxo-1H-pyrrolo[1,2-c]imidazoles
IN Taylor, Eric Deguyon; Petrov, Viacheslav Alexandrovich; Schaefer, Matthias; Drauz, Karlheinz; Vogt, Anne; Weckbecker, Christoph; Swearingen, Steven H.; Kamireddy, Balreddy
PA E. I. Du Pont de Nemours & Co., USA; Degussa A.-G.
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9837065	A1	19980827	WO 1998-US2721	19980213
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	IN 1998CA00208	A	20051118	IN 1998-CA208	19980209
	ZA 9801168	A	19990812	ZA 1998-1168	19980212
	CA 2276056	A1	19980827	CA 1998-2276056	19980213
	AU 9861604	A	19980909	AU 1998-61604	19980213
	EP 973739	A1	20000126	EP 1998-906363	19980213
	EP 973739	B1	20051102		
	R: DE, FR, IT				
	BR 9807256	A	20000502	BR 1998-7256	19980213
	US 6384234	B1	20020507	US 1999-367899	19991230
	US 2002137946	A1	20020926	US 2002-35136	20020104
	US 6664400	B2	20031216		
PRAI	US 1997-38429P	19970219			
	WO 1998-US2721	19980213			
	US 1999-367899	19991230			

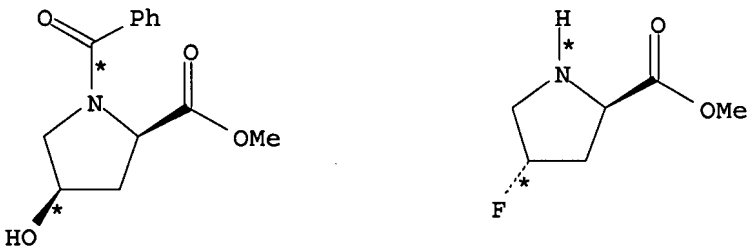
OS MARPAT 129:202944
GI



I

AB Title compds. [I; R1 = haloalkyl, alkoxyalkyl, cyanoalkyl, etc.; R2 = H, (halo)alkyl, alkanoyl, alkoxycarbonyl, etc.; R3 = H or OH; R4,X = H, F, Cl; Y = F or Cl; R5 = OH; R6 = H; R5R6 = bond] were prepared Thus, N-(2-chloro-4-fluoro-5-isocyanatophenyl)chloromethanesulfonamide (preparation given) was amidated by cis-4-hydroxy-D-proline to give I (R1 = Y = Cl, R2 = H, X = F)(II; R4 = R6 = H, R3 = R5 = OH) which was cyclized and the product fluorinated to give II (R3 = H, R4 = F, R5R6 = bond).

RX(9) OF 34 ...AB ===> AE...



AB

AE
YIELD 80%

RX(9) RCT AB 212198-48-6

STAGE(1)
RGT W 309-88-6 Ishikawa reagent
SOL 75-09-2 CH2Cl2, 108-88-3 PhMe

STAGE(2)
RGT I 7647-01-0 HCl
SOL 7732-18-5 Water

PRO AE 131176-03-9
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> => d que l9 stat
L4            89 SEA FILE=CAPLUS ABB=ON  PLU=ON  "TOMISAWA KAZUYUKI"/AU
L5             1 SEA FILE=CAPLUS ABB=ON  PLU=ON  "TATSUTA DAI"/AU
L6             2 SEA FILE=CAPLUS ABB=ON  PLU=ON  "YOSHIDA TOMOMICHI"/AU
L7            61 SEA FILE=CAPLUS ABB=ON  PLU=ON  "YOKOO CHIHIRO"/AU
L8           150 SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 OR L5 OR L6 OR L7
L9             1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND (FLUORO(L)PROLINE OR
                 FLUOROPROLINE OR FLUORO(W)PROLINE)

=> d bib abs
```

L9 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:158636 CAPLUS
DN 142:261782
TI Process for preparation of cis-4-fluoro-L-proline derivatives
IN Tomisawa, Kazuyuki; Tatsuta, Dai; Yoshida, Tomomichi; Yokoo, Chihiro
PA Taisho Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005016880	A1	20050224	WO 2004-JP11827	20040818
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004265182	A1	20050224	AU 2004-265182	20040818
CA 2534884	A1	20050224	CA 2004-2534884	20040818
EP 1657237	A1	20060517	EP 2004-771788	20040818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1839120	A	20060927	CN 2004-80023726	20040818
NO 2006000703	A	20060313	NO 2006-703	20060214
US 2006281927	A1	20061214	US 2006-568708	20060804
PRAI JP 2003-207718	A	20030818		
WO 2004-JP11827	W	20040818		

OS CASREACT 142:261782; MARPAT 142:261782
AB This invention pertains to a method for producing high purity cis-4-fluoro-L-proline derivs., which comprises reacting a trans-4-hydroxy-L-proline derivative with N,N-diethyl-N-(1,1,2,3,3,3-hexafluoropropyl)amine in the presence of a HF scavenger. For example, (2S,4R)-1-(tert-butoxycarbonyl)-4-hydroxypyrrolidine-2-carboxylic acid Me ester was reacted with N,N-diethyl-N-(1,1,2,3,3,3-hexafluoropropyl)amine in CH2Cl2 in the presence of NaF to give (2S,4S)-1-(tert-butoxycarbonyl)-4-fluoropyrrolidine-2-carboxylic acid Me ester. This invention provides a convenient method to prepare cis-4-fluoro-L-proline derivs. in high yield under mild conditions at low cost.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> d his full

     (FILE 'HOME' ENTERED AT 14:23:27 ON 23 MAY 2007)

     FILE 'CASREACT' ENTERED AT 14:23:44 ON 23 MAY 2007
L1             STRUCTURE UPLOADED
               D
L2           0 SEA SSS SAM L1 (     0 REACTIONS)
L3           3 SEA SSS FUL L1 (    10 REACTIONS)
               D QUE L3 STAT
               D 1-3 BIB ABS FHIT

     FILE 'CAPLUS' ENTERED AT 14:29:43 ON 23 MAY 2007
               E TOMISAWA KAZUYUKI/AU
L4          89 SEA ABB=ON  PLU=ON  "TOMISAWA KAZUYUKI"/AU
               E TATSUTA DAI/AU
L5           1 SEA ABB=ON  PLU=ON  "TATSUTA DAI"/AU
               E YOSHIDA TOMOMICHI/AU
L6           2 SEA ABB=ON  PLU=ON  "YOSHIDA TOMOMICHI"/AU
               E YOKOO CHIHIRO/AU
L7          61 SEA ABB=ON  PLU=ON  "YOKOO CHIHIRO"/AU
L8         150 SEA ABB=ON  PLU=ON  L4 OR L5 OR L6 OR L7
L9           1 SEA ABB=ON  PLU=ON  L8 AND (FLUORO(L)PROLINE OR FLUOROPROLINE
               OR FLUORO(W)PROLINE)
               D QUE L9 STAT
               D BIB ABS


     FILE HOME

     FILE CASREACT
     Copyright of the articles to which records in this database refer is
     held by the publishers listed in the PUBLISHER (PB) field (available
     for records published or updated in Chemical Abstracts after December
     26, 1996), unless otherwise indicated in the original publications.

     FILE CONTENT:1840 - 19 May 2007 VOL 146 ISS 22

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     ******************************************************
     *                                                    *
     *     CASREACT now has more than 12 million reactions*
     *                                                    *
     ******************************************************

     Some CASREACT records are derived from the ZIC/VINITI database (1974-1999)
     provided by InfoChem, INPI data prior to 1986, and Biotransformations
     database compiled under the direction of Professor Dr. Klaus Kieslich.

     This file contains CAS Registry Numbers for easy and accurate substance
     identification.

     FILE CAPLUS

     Copyright of the articles to which records in this database refer is
     held by the publishers listed in the PUBLISHER (PB) field (available
     for records published or updated in Chemical Abstracts after December
     26, 1996), unless otherwise indicated in the original publications.
     The CA Lexicon is the copyrighted intellectual property of the
     American Chemical Society and is provided to assist you in searching
     databases on STN.  Any dissemination, distribution, copying, or storing
     of this information, without the prior written consent of CAS, is
```

strictly prohibited.

FILE COVERS 1907 - 23 May 2007 VOL 146 ISS 22
FILE LAST UPDATED: 22 May 2007 (20070522/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=>